DETAILED ACTION

1. According to a preliminary amendment filed on Oct. 3, 2005, the applicants have canceled claims 1-10 and furthermore, have added new claims 11-20.

2. Claims 11-20 are now pending in the application.

Election/Restrictions

3. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 16, 17, 20 and in part 11-15, 18 and 19, drawn to methods of treatment where growth hormone secretagogue is represented by compounds of formula I or II (see page 8 of specification).

Group II, claim(s) In part 11-15, 18 and 19, drawn to methods of treatment where growth hormone secretagogue is represented by compounds of formula III, IV or IX (see pages 9 and 11 of specification).

Group III, claim(s) In part 11-15, 18 and 19, drawn to methods of treatment where growth hormone secretagogue is represented by compounds of formula III, IV or IX (see pages 9 and 11 of specification).

Group IV, claim(s) In part 11-15, 18 and 19, drawn to methods of treatment where growth hormone secretagogue is represented by compounds of formula V (see page 9 of specification).

Group V, claim(s) In part 11-15, 18 and 19, drawn to methods of treatment where growth hormone secretagogue is represented by compounds of formula VI (see page 10 of specification).

Group VI, claim(s) In part 11-15, 18 and 19, drawn to methods of treatment where growth hormone secretagogue is represented by compounds of formula VI (see page 10 of specification).

Group VII, claim(s) In part 11-15, 18 and 19, drawn to methods of treatment where growth hormone secretagogue is represented by compounds of formula VII (see page 10 of specification).

Group VIII, claim(s) In part 11-15, 18 and 19, drawn to methods of treatment where growth hormone secretagogue is represented by compounds of formula VIII (see page 11 of specification).

Group IX, claim(s) In part 11-15, 18 and 19, drawn to methods of treatment where growth hormone secretagogue is represented by compounds of formula X (see page 12 of specification).

4. The inventions listed as Groups I through IX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

There is no common core which in the Markush Practice, is a significant structural element shared by all of the alternatives; see PCT Administrative Instructions Annex B Part I (f) (i) (B) (1).

5. During a telephone conversation with the applicant's attorney, Mr. J. Eric Thies on April 15, 2008, a provisional election was made with traverse to prosecute the invention of group I, claims 16, 17, 20 and in part 11-15, 18 and 19. Affirmation of this election must be made by applicant in replying to this Office action.

Specification

6. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 11-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight different factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, state of the prior art, unpredictability and the breadth of claims.

In regard to preventing dementia, Alzheimer's disease, cognitive impairment or deposition of beta-amyloid in the brain, there is no teaching either in the specification or prior art that decreased levels of growth hormone are solely responsible for the etiology of dementia, Alzheimer's disease, cognitive impairment or deposition of beta-amyloid in the brain. There are no working examples present showing complete prevention of memory loss in animal models of dementia, Alzheimer's disease or cognitive impairment by combination of any compounds. It is well known in the art that there are multiple mechanisms involved in the etiology of any known disease condition including

dementia, Alzheimer's disease and cognitive impairment. Therefore, correcting only one of these several mechanisms such as enhancing growth hormone and inhibiting PDE4 will not prevent or completely cure that disease condition. Thus, in absence of such teachings, guidance and presence of working examples, it would require undue experimentation to demonstrate efficacy of instant compounds of formulae I and II in combination with thousands of known PDE4 inhibitors for preventing memory loss in animal models of dementia, Alzheimer's disease or cognitive impairment and hence their utility for preventing these disease conditions.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 11-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shearman (WO 2004/080459) in view of Guay (WO 03/018579, cited on applicant's form 1449).

Shearman teaches methods of treating cognitive impairment, Alzheimer disease, dementia by growth hormone secretagogue of formula (I). Shearman meets all the limitations of instant claims except that it does not teach combining the compounds of formula (I) with PDE4 inhibitor for treating these disease conditions. However, Guay (WO 03/018579) teaches utility of PDE4 inhibitors in treating memory impairment and Alzheimer disease (see claim 24 as well as compounds in claim 13, specifically compound in lines 22-24). Therefore, it would have been obvious to one skilled in the art to combine PDE4 inhibitor with the compounds of formula (I) for treating cognitive impairment, Alzheimer disease and dementia with reasonable expectation of success to enhance efficacy of combination treatment as compared to compounds of formula (I) alone.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571)272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Charanjit S. Aulakh/
Primary Examiner, Art Unit 1625